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Registration Decision

RD2010-16

Garlic Oil

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Registration Decision for Garlic Oil

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, and Regulations, is granting full registration for the sale and use of Garlic Oil FCC 8170 and Comfort Zone containing the technical grade active ingredient garlic oil to repel mosquitoes outdoors.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document¹ Proposed Registration Decision PRD2010-07, *Garlic Oil*. This Registration Decision² describes this stage of the PMRA's regulatory process for garlic oil and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2010-07.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2010-07, *Garlic Oil* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable³ if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value⁴ when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

¹ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

² "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

³ "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

⁴ "Value" as defined by subsection 2(1) of *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra

What is Garlic Oil?

Garlic oil is an extract of garlic (*Allium sativum*). In the end-use product, Comfort Zone, it is formulated to be water-soluble. Garlic contains a high concentration of sulphur compounds, only some of which contribute to its characteristic odour. Garlic is known to be repellent to various insects, however the exact mode of action of this repellency is unknown.

Health Considerations

Can Approved Uses of Garlic Oil Affect Human Health?

Garlic oil is unlikely to affect your health when used according to label directions.

Exposure to garlic oil may occur when handling and applying the end-use product, Comfort Zone, as well as during typical residential activities following application. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

The technical grade active ingredient, garlic oil, is of slight acute toxicity by the oral route, low acute toxicity by the dermal route, a severe skin irritant, a moderate eye irritant, and a dermal sensitizer. Because garlic is a known mucosal irritant, inhalation of garlic oil mist or vapour may result in throat and respiratory tract irritation. The end-use product, Comfort Zone, is of low acute toxicity by both the oral and dermal route, may be a skin and eye irritant, and a possible dermal sensitizer. Cautionary statements alerting the user to garlic oil's acute toxicity, skin and eye irritation, and dermal sensitization are required on the technical grade active ingredient product label, as well as Comfort Zone being a possible skin and eye irritant, and a dermal sensitizer.

Inhalation, dermal, and ocular exposures are possible when applying the product, particularly to the applicator and bystanders located near the treatment area. Also, entry into a recently sprayed area may result in dermal exposure. Therefore, spray advisory and restricted entry statements are required on the end-use product label to minimize applicator and bystander exposures.

The data requirements for short-term toxicity, prenatal developmental toxicity, and genotoxicity were waived by the PMRA based on the long history of safe consumption of garlic as a whole foodstuff and garlic oil in natural health products.

Residues in Water and Food

Dietary risks from food and water are not of concern.

The proposed use pattern for Comfort Zone is for non-food situations. Garlic oil readily degrades in the environment, so any inadvertent exposure of garlic oil to food, feed, or water from drift or direct contact is not expected to result in any dietary risk.

Risks From Handling Garlic Oil

Risks are not of concern when Comfort Zone is used according to label directions, which include protective measures.

Domestic users handling and applying Comfort Zone to areas that attract mosquitoes, such as plants, shrubs, turf, and under decks, can come in direct contact with garlic oil on the skin and in the eyes. Following the precautionary label statements aimed at minimizing exposure to the product will ensure domestic users are appropriately protected. Potential for inhalation of garlic oil while handling and applying the end-use product is anticipated to be negligible if users observe the precautionary label statements.

Accidental bystander exposure is possible from spray drift, but exposure is expected to be negligible if the precautionary label statements are observed by the applicator.

Post-application exposure is possible in individuals who immediately enter freshly treated areas. The transfer of garlic oil from turf or foliar application to an individual who is not sensitive to garlic will not pose a health concern.

Environmental Considerations

What Happens When Garlic Oil, as part of the End-Use Product Comfort Zone, Is Introduced Into the Environment?

Garlic oil is not expected to pose significant environmental risk when used according to label directions.

Garlic oil is expected to degrade rapidly in the environment. Garlic oil is a naturally occurring compound, and is considered non-toxic from an environmental perspective because it acts as a repellent. Environmental exposure is expected to be minimal when used according to the label directions.

Value Considerations

What Is the Value of Comfort Zone?

Comfort Zone is an insect repellent for mosquitoes.

Comfort Zone is a product for domestic use containing 4% Garlic oil for application on grass, plants, shrubs and under decks and porches. The product repels mosquitoes from these areas for up to five days.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Comfort Zone to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

The statements, "MAY BE A SKIN AND EYE IRRITANT" and "POTENTIAL SKIN SENSITIZER" have been included on the principal display panel of the label and "Do not swallow", "Avoid getting on skin and in eyes", "May cause skin and eye irritation", "Avoid inhaling/breathing mist or vapours", and "Potential skin sensitizer" have been included in the PRECAUTIONS section of the secondary display panel of the end-use product label.

Because some individuals may be sensitive or allergic to garlic, the statements, "Apply only when the potential for drift is minimal", "Individuals who are sensitive or allergic to garlic should avoid handling Comfort Zone" and "Individuals who are sensitive or allergic to garlic should avoid treated areas until dry or until after a heavy rain" have also been included in the PRECAUTIONS section of the secondary display panel of the label.

Other Information

The relevant test data on which the decision is based (as referenced in this document) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

Any person may file a notice of objection⁵ regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of Health Canada's website (Request a Reconsideration of Decision, healthcanada.gc.ca/pmra) or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

⁵ As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Comments and Responses

1. A comment was received that indicated that information related to the end-use product, Comfort Zone, was absent in the proposed registration decision document posted on the Health Canada website. Information, such as the ingredients of Comfort Zone, application instructions (pest, location and equipment), and what it potentially may be mixed with prior to application, were requested.

Response: The document that was published on the Health Canada website (www.hc-sc.gc.ca) during the consultation period was a high level summary of the Garlic Oil consultation document. As per the instructions provided on the website, a full copy of the Proposed Registration Decision document (*Garlic Oil* - PRD2010-07) can be obtained by contacting publications@hc-sc.gc.ca. The full document includes end-use product information, such as the active ingredient, its properties and uses and directions for use. Comfort Zone is a ready-to-use garlic solution that is not mixed with any additional ingredients prior to application. The directions for use are as follows: For best results, spray in early morning or early evening. Spray until run-off. Use in areas that attract mosquitoes such as grass, plants, shrubs and under decks and porches. The repelling effect of Comfort Zone lasts up to 5 days. Re-apply after heavy rain or if mosquitoes continue to be a problem.

2. A comment was received that expressed concern regarding products that may be applied to water. It was requested that assurances be given to protect water and to ensure the consumer has the extra knowledge required for their successful use.

Response: Application to water is not listed as one of the accepted use sites on the Comfort Zone label. Additionally, the statement "DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes" is included on the Comfort Zone label.

3. A comment was received that questioned the adequacy of the one efficacy trial, with one replicate in a household setting evaluated for the registration of Comfort Zone. Concern was expressed that this is significantly less data than would be required for a conventional chemical, especially for protection from mosquitoes, which are a public health pest. It was also indicated that it was unclear whether the trial was conducted in Canada or on relevant mosquito species.

Response: Comfort Zone is not a personal mosquito repellent, and it is not intended to replace a personal insect repellent. It is an area repellent, i.e., it repels mosquitoes from certain outdoor areas, when applied to plants, shrubs and turf in that area. The label claim—that the product repels mosquitoes for up to 5 days from certain outdoor areas when applied to plants shrubs and turf in those areas—was supported by the efficacy data. The number of acceptable efficacy trials can be dependent on several factors, such as the number of habitats represented, and is not necessarily defined by an exact number. In this case, one trial was accepted to support these claims because it was conducted in two habitats. It was conducted outdoors in two locations: on a golf course, and in a lot containing trees and shrubs beside a river. This trial was conducted close to

Charlottetown in Prince Edward Island, Canada, and therefore, the data collected are pertinent to Canadian mosquito species.

4. A comment was received concerning the levels of reduction in populations achieved in the efficacy trial compared to the control trial. It was noted that repellency is a very strong claim that is normally associated with on-skin repellents that require 95% repellency in humans. It was suggested that the use of the term repels may not be appropriate for this product type, since human subjects were not used to determine repellency and mosquito traps were used to monitor populations. It was also suggested that only a softer claim like "reduces annoyance from mosquitoes" or "reduces populations" should be permitted.

Response: The Comfort Zone label carries the claim that mosquitoes would be repelled and this claim was evaluated. The PMRA does not reserve the claim of "repel" solely for "on skin products" but for any product that has data demonstrating it repels a certain pest from a subject or area. Although the efficacy data submitted did not indicate that the product reduced populations, it did demonstrate that it repelled mosquitoes from a treated area. Human subjects are not required for studies to support this use pattern on the Comfort Zone label. PMRA considers data collected using mosquito traps are adequate to support this type of use.

5. A comment was received regarding the fact that the use of the claim "repels mosquitoes for up to 5 days" on the label may also cause confusion for consumers, leading them to think that this product is for on-skin application. As the product is a potential skin sensitizer, it was suggested that the label use very clear wording to avoid confusion for consumers.

Response: The PMRA is satisfied that the Comfort Zone label statements adequately address concerns regarding the directions for use of this end-use product. Comfort Zone is an area insect repellent. The directions for use state that Comfort Zone is for "Use in areas that attract mosquitoes such as grass, plants, shrubs, and under decks and porches." The precautionary statements on the Comfort Zone label clearly indicate that this product is a "Potential skin sensitizer" and "May be a skin irritant" on the front page of the label. It also states to "Avoid getting on skin..." in the Precautions section and has first aid recommendations in the case that skin is exposed.

6. An analytical method was not required for the active ingredient or the end use formulation. A comment was received questioning how the PMRA can fully characterize and analyze the end use product to verify the label guarantee and to fully characterize the material as is normally required by the formulators policy.

Response: The active ingredient for this product is 100% Garlic Oil, which is a complex mixture of compounds that are not easily characterized or quantifiable. The applicant submitted product specifications, which show that the product meets Food Chemicals

Codex (FCC) specifications. For products which are of food grade and meet FCC specifications, analytical methods are not required (*Guidelines for the Registration of Low-Risk Biochemicals and Other Non-Conventional Pesticides* - PRO2007-02).

7. A comment was received concerning whether stability data were received for the end use product formulation to ensure that Comfort Zone would not damage the container over time.
8. The end-use product contains 4% Garlic Oil. The applicant has reported that there was no indication that the product was corrosive, when stored at ambient temperature in a sealed plastic container. Additional data to support these comments were not required, since the active (garlic oil) is of food grade and meets the Food Chemicals Codex (FCC) specification.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number: 1594643

Reference: Manufacturing Methods for the TGAI, DACO: 2.11 **CBI**

PMRA Document Number: 1594644

Reference: Chemical and Physical Properties for AIC, DACO: 2.14 **CBI**

PMRA Document Number: 1594645

Reference: Properties for the TGAI, DACO: 2.14.1 **CBI**

PMRA Document Number: 1594649

Reference: Properties for the TGAI, DACO: 2.14.2 **CBI**

PMRA Document Number: 1594651

Reference: Properties for the TGAI, DACO: 2.14.3 **CBI**

PMRA Document Number: 1594652

Reference: DACO 2.14.6 Chemical and Physical Properties, DACO: 2.14.6 **CBI**

PMRA Document Number: 1594653

Reference: Water Solubility (mg/L), DACO: 2.14.7 **CBI**

PMRA Document Number: 1594654

Reference: Solvent Solubility (mg/L), DACO: 2.14.8 **CBI**

PMRA Document Number: 1594656

Reference: Properties for the TGAI, DACO: 2.15 **CBI**

PMRA Document Number: 1594657

Reference: Properties for the TGAI, DACO: 2.16 **CBI**

PMRA Document Number: 1679580

Reference: 2008, Odour, DACO: 3.5.3 **CBI**

PMRA Document Number: 1679581

Reference: 2008, Formulation type, DACO: 3.5.4 **CBI**

PMRA Document Number: 1679582

Reference: 2008, Bottle Specifications, DACO: 3.5.5 **CBI**

PMRA Document Number: 1679583
Reference: 2008, Density or specific gravity, DACO: 3.5.6 **CBI**

PMRA Document Number: 1679584
Reference: 2008, pH, DACO: 3.5.7 **CBI**

PMRA Document Number: 1679585
Reference: 2008, Oxidizing and Reducing, DACO: 3.5.8 **CBI**

PMRA Document Number: 1679586
Reference: 2008, Viscosity, DACO: 3.5.9 **CBI**

PMRA Document Number: 1679609
Reference: 2008, Manufacturing methods, DACO: 2.11.1, 2.11.2, 2.11.3, 2.11.4, 2.12, 2.13 **CBI**

PMRA Document Number: 1778107
Reference: 2008, Certificate of Analysis, DACO: 2.13.2 **CBI**

PMRA Document Number: 1778114
Reference: Product Specification Sheet, Ecom Industries Inc. **CBI**

PMRA Document Number: 1594602
Reference: Impurities of Toxicological Concern, DACO: 3.4.2 **CBI**

PMRA Document Number: 1594603
Reference: Colour, DACO: 3.5.1

PMRA Document Number: 1679579
Reference: 2008, Physical State, DACO: 3.5.2 **CBI**

PMRA Document Number: 1832111
Reference: 2009, Formulation Process, DACO: 3.2.2 **CBI**

2.0 Human and Animal Health

PMRA Document Number: 1594606
Reference: Summaries, DACO: 5.1

PMRA Document Number: 1594607
Reference: Other studies/Data/Reports, DACO: 5.14

PMRA Document Number: 1594658
Reference: TOXICOLOGY, DACO: 4.1

PMRA Document Number: 1594661

Reference: 1992, US EPA, Foreign Reviews, DACO: M12.5

PMRA Document Number: 1763339

Reference: 2009, Material Safety data Sheet, DACO: 0.9, 2.14.1, 2.14.2, 2.14.3, 2.14.6, 2.2, 2.3, 2.3.1, 2.5, 2.6, 2.7, 2.8, 2.9

PMRA Document Number: 1854234

Reference: DACO 5.2 - New Discussion for Garlic Oil Use Description/Scenario (Application and Post Application), DACO: 5.2

3.0 Value

PMRA Document Number: 1594610

Reference: Value Summaries, DACO: 10.1

PMRA Document Number: 1594611

Reference: Efficacy Studies, Mode of Action, DACO: 10.2

PMRA Document Number: 1594612

Reference: Mode of Action, DACO: 10.2.1

PMRA Document Number: 1594613

Reference: Description of Pest Problem, DACO: 10.2.2

PMRA Document Number: 1594614

Reference: EFFICACY TRIALS, DACO: 10.2.3

PMRA Document Number: 1594615

Reference: Efficacy of An Area Repellent against Mosquitoes, DACO: 10.2.1, 10.2.3.3, 10.3.1, 10.4, 10.5

PMRA Document Number: 1594616

Reference: Adverse Effects on Use Site, DACO: 10.3

PMRA Document Number: 1594617

Reference: Survey of Alternatives (chemical and non-chemical), DACO: 10.5.1

PMRA Document Number: 1679575

Reference: 2008, Summary, DACO: 10.1

PMRA Document Number: 1679576

Reference: 2008, Mode of Action, DACO: 10.2.1

PMRA Document Number: 1679577

Reference: 2008, 10.3.1 Summary, DACO: 10.3.1

PMRA Document Number: 1679595
2008, Efficacy of an Area Repellent against mosquitoes modified, DACO: 10.2.3

PMRA Document Number: 1807203
Reference: 1998, <http://file:///C:/BRC A%20Documents/Corporate%20Documents/Operation%20Blackberr...> 12/3/2005, Garlic Patent, Mosquito Repelling Technique, US Patent # 5,733,552 Current U.S. Class: 424/754 Intern'l Class: A61K 035/78, DACO: 10.2

PMRA Document Number: 1807207
Reference: 1995, MOSQUITO BARRIER Tests of Mosquito Barrier® Garlic Juice, DACO: 10.2

B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

PMRA Document Number: 1859677
Reference: Chapter 8 Garlic Forensic Science and Medicine, Herbal Products: Toxicology and Clinical Pharmacology, Second Edition., DACO: 4.8

PMRA Document Number: 1860488
Reference: RTECS Registry of Toxic Effects of Chemical Substances Allyl disulfide, Canadian Centre for Occupational Health & Safety, DACO: 4.2.1, 4.2.2, 4.2.4, 4.2.5, 4.3.1, 4.5.4, 4.5.5

PMRA Document Number: 1860536
Reference: Fragrance raw materials monographs DIALLYL DISULPHIDE, DACO: 4.2.1, 4.2.2, 4.2.5, 4.2.6, 4.5.4, 4.5.5

PMRA Document Number: 1860541
Reference: Fragrance raw materials monographs DIALLYL SULPHIDE, DACO: 4.2.1, 4.2.2, 4.2.5, 4.2.6, 4.5.4, 4.5.5

PMRA Document Number: 1861150
Reference: 2003, Rules and Regulation Diallyl Sulfides; Exemption from the Requirement of a Tolerance, Federal Register Vol. 68, No. 131, DACO: 4.8

PMRA Document Number: 1861165
Reference: RTECS Registry of Toxic Effects of Chemical Substances - Garlic Oil, Canadian Centre for Occupational Health and Safety, DACO: 4.2.1, 4.3.1

PMRA Document Number: 1861167
Reference: ChemIDplus Advanced Allyl sulfide, United States National Library of Medicine, DACO: 4.2.1

PMRA Document Number: 1861180

Reference: Garlic oil china 8000-78-0 *Allium sativum* l. bulb oil, DACO: 4.8

PMRA Document Number: 1861197

Reference: ChemIDplus Advanced Allyl sulfide, U.S. National Library of Medicine, DACO: 4.2.1, 4.2.2

PMRA Document Number: 1861206

Reference: ChemIDplus Advanced Diallyl disulfide, U.S. National Library of Medicine, DACO: 4.2.1, 4.2.2

PMRA Document Number: 1864853

Reference: 2004 TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices., DACO: 4.8